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NEWS 4	Jul 30	BEILSTEIN on STN workshop to be held August 24 in conjunction with the 228th ACS National Meeting
NEWS 5	AUG 02	IFIPAT/IFIUDB/IFICDB reloaded with new search and display fields
NEWS 6	AUG 02	CAplus and CA patent records enhanced with European and Japan Patent Office Classifications
NEWS 7	AUG 02	The Analysis Edition of STN Express with Discover! (Version 7.01 for Windows) now available
NEWS 8	AUG 04	Pricing for the Save Answers for SciFinder Wizard within STN Express with Discover! will change September 1, 2004
NEWS 9	AUG 27	BIOCOMMERCE: Changes and enhancements to content coverage
NEWS 10	AUG 27	BIOTECHABS/BIOTECHDS: Two new display fields added for legal status data from INPADOC
NEWS 11	SEP 01	INPADOC: New family current-awareness alert (SDI) available
NEWS 12	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
NEWS 13	SEP 01	New display format, HITSTR, available in WPIDS/WPINDEX/WPIX
NEWS 14	SEP 14	STN Patent Forum to be held October 13, 2004, in Iselin, NJ

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NEWS HOURS	STN Operating Hours Plus Help Desk Availability
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FILE 'HOME' ENTERED AT 15:00:16 ON 22 SEP 2004

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=> file reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                          ENTRY    SESSION
FULL ESTIMATED COST                                        0.21       0.21

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STRUCTURE FILE UPDATES:   21 SEP 2004  HIGHEST RN 749178-43-6
DICTIONARY FILE UPDATES:  21 SEP 2004  HIGHEST RN 749178-43-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

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Experimental and calculated property data are now available. For more
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http://www.cas.org/ONLINE/DBSS/registryss.html

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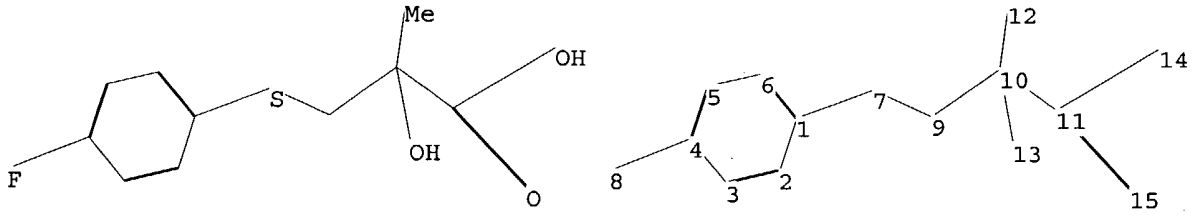


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7  8  9  10  11  12  13  14  15
ring nodes :
1  2  3  4  5  6
chain bonds :
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ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6
exact/norm bonds :
1-7  7-9  10-13
exact bonds :
4-8  9-10  10-11  10-12
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6  11-14  11-15
isolated ring systems :
containing 1 :


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:CLASS  8:CLASS  9:CLASS  10:CLASS
 11:CLASS  12:CLASS  13:CLASS  14:CLASS  15:CLASS
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L1 STRUCTURE UPLOADED

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SAMPLE SCREEN SEARCH COMPLETED - 1 TO ITERATE

100.0% PROCESSED 1 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

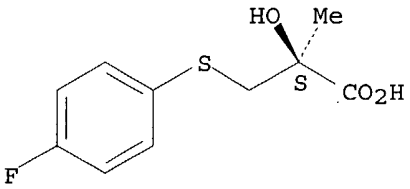
FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 1 TO 80
PROJECTED ANSWERS: 1 TO 80

L2 1 SEA SSS SAM L1

=> d scan

L2 1 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Propanoic acid, 3-[(4-fluorophenyl)thio]-2-hydroxy-2-methyl-, (2S)- (9CI)
MF C10 H11 F O3 S
CI COM

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=> s l1 ful
FULL SEARCH INITIATED 15:00:55 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 25 TO ITERATE

100.0% PROCESSED 25 ITERATIONS 6 ANSWERS
SEARCH TIME: 00.00.01

L3 6 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 155.42 155.63

FILE 'CAPLUS' ENTERED AT 15:01:01 ON 22 SEP 2004

FILE COVERS 1907 - 22 Sep 2004 VOL 141 ISS 13
FILE LAST UPDATED: 21 Sep 2004 (20040921/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 7 L3

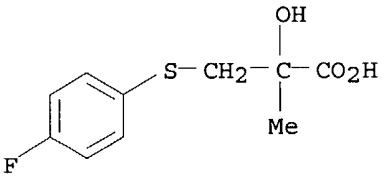
=> d l4 ibib hitstr abs 1-7

L4 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:182593 CAPLUS
DOCUMENT NUMBER: 140:235504
TITLE: Preparation and crystallization of bicalutamide
INVENTOR(S): Dolitzky, Ben-Zion; Reany, Ofer; Shammai, Jenny
PATENT ASSIGNEE(S): Israel
SOURCE: U.S. Pat. Appl. Publ., 12 pp., Cont.-in-part of U.S. Ser. No. 170,721.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004044249	A1	20040304	US 2003-606403		20030625
US 2003045741	A1	20030306	US 2002-170721		20020613
US 6737550	B2	20040518			
US 2004059147	A1	20040325	US 2003-668982		20030922
US 2004167349	A1	20040826	US 2004-791468		20040301
US 2004176633	A1	20040909	US 2004-796313		20040308
US 2004176638	A1	20040909	US 2004-796822		20040308
PRIORITY APPLN. INFO.:			US 2001-298009P	P	20010613
			US 2002-371069P	P	20020409
			US 2002-170721	A2	20020613

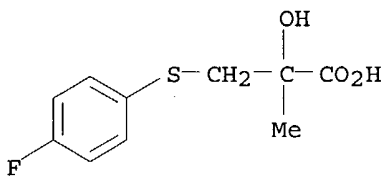
OTHER SOURCE(S): CASREACT 140:235504
IT **339530-91-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, micronization and crystallization of bicalutamide)
RN 339530-91-5 CAPLUS
CN Propanoic acid, 3-[(4-fluorophenyl)thio]-2-hydroxy-2-methyl- (9CI) (CA

INDEX NAME)



AB Racemic N-[4-cyano-3-trifluoromethylphenyl]-3-[4-fluorophenylsulfonyl]-2-hydroxy-2-methylpropionamide (bicalutamide) was prepared starting from Et pyruvate and Me methacrylate. Thus, 5-amino-2-cyanobenzotrifluoride was treated with DABCO and reacted with deprotonated Et 2-(4-fluorophenylsulfonyl)-2-hydroxy-2-methylpropionate (prepared from Et pyruvate) to give 40% bicalutamide. Micronized particles of bicalutamide can be obtained as pharmaceutical compns. that are useful for its anti-androgen activity (no data). Bicalutamide intermediates were also prepared, including Et 2-(4-fluorophenylsulfonyl)-2-hydroxy-2-methylpropionate, Me 2,3-epoxy-2-methylpropionate and 2-hydroxy-2-methyl-3-(4-fluorophenylthio)propionic acid. The present invention further discloses the isolation and purification of bicalutamide by various crystallization methods.

L4 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:790626 CAPLUS
DOCUMENT NUMBER: 140:270600
TITLE: Synthesis of bicalutamide
AUTHOR(S): Xiao, Tao; Zhang, Xiao-qing; Tian, Chun-mei; Wang, Jin-tang
CORPORATE SOURCE: Department of Applied Chemistry, Nanjing University of Chemical Technology, Nanjing, 210009, Peop. Rep. China
SOURCE: Hecheng Huaxue (2003), 11(4), 346-348
CODEN: HEHUE2; ISSN: 1005-1511
PUBLISHER: Hecheng Huaxue Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 140:270600
IT **339530-91-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of bicalutamide)
RN 339530-91-5 CAPLUS
CN Propanoic acid, 3-[(4-fluorophenyl)thio]-2-hydroxy-2-methyl- (9CI) (CA INDEX NAME)



AB Bicalutamide was synthesized from Me methacrylate via oxidation, condensation with 4-fluorothiophenol and hydrolysis to give α-hydroxy acid which was first reacted with 2-trifluoromethyl-4-aminobenzonitrile and then

oxidized with m-chloroperoxybenzoic acid. The overall yield was about 11.2%.

L4 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:964133 CAPLUS
DOCUMENT NUMBER: 138:24551
TITLE: Preparation of rac-bicalutamide
INVENTOR(S): Dolitzky, Ben-Zion; Reany, Ofer; Shamai, Jenny
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.; Biogal Gyogyszergyar
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

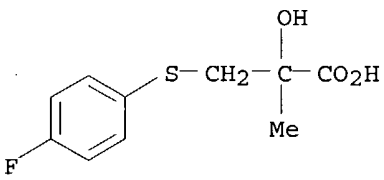
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002100339	A2	20021219	WO 2002-US18329	20020613
WO 2002100339	A3	20031016		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1406855	A2	20040414	EP 2002-739801	20020613
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.:
US 2001-298009P P 20010613
US 2002-371069P P 20020409
WO 2002-US18329 W 20020613

OTHER SOURCE(S): CASREACT 138:24551

IT **339530-91-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of rac-bicalutamide)

RN 339530-91-5 CAPLUS
CN Propanoic acid, 3-[(4-fluorophenyl)thio]-2-hydroxy-2-methyl- (9CI) (CA INDEX NAME)

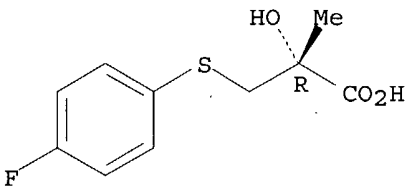


AB Racemic and optically active N-[4-cyano-3-trifluoromethylphenyl]-3-[4-fluorophenylsulfonyl]-2-hydroxy-2-Me propionamide (bicalutamide) were prepared starting from Et pyruvate and Me methacrylate. Thus, 5-amino-2-cyanobenzotrifluoride was treated with DABCO and reacted with deprotonated ethyl-[2-(4-fluorophenyl sulfone)]-2-hydroxy propionate

(prepared from Et pyruvate) to give %40 rac-bicalutamide. Micronized particles of rac-bicalutamide can be obtained as pharmaceutical compns. that are useful for its anti-androgen activity (no data). Bicalutamide intermediates were also prepared, including ethyl-[2-(4-fluorophenyl sulfone)]-2-hydroxy propionate, 1,2-epoxy-2-Me propionate and 2-hydroxy-2-methyl-3-(4-fluorophenylthio) propionic acid.

L4 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:509907 CAPLUS
DOCUMENT NUMBER: 137:384623
TITLE: Syntheses of enantiomerically pure (R)- and (S)-bicalutamide
AUTHOR(S): James, Kenneth D.; Ekwuribe, Nnochiri N.
CORPORATE SOURCE: Department of Innovation, Nobex Corporation, Durham, NC, 27713, USA
SOURCE: Tetrahedron (2002), 58(29), 5905-5908
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:384623
IT **335595-52-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(syntheses of enantiomerically pure (R)- and (S)-bicalutamide)
RN 335595-52-3 CAPLUS
CN Propanoic acid, 3-[(4-fluorophenyl)thio]-2-hydroxy-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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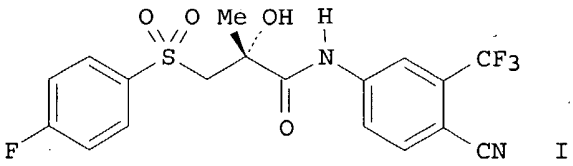

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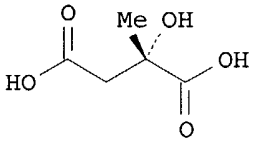


II

AB The racemic antiandrogen bicalutamide is the leading antiandrogen used for the treatment of prostate cancer. The (R)-isomer possesses virtually all of the activity, but both isomers are metabolized by the liver. A convenient synthetic route to the active enantiomer would be an attractive option for patients who are hepatically impaired. We now demonstrate a rather short synthesis of (R)-bicalutamide (I), starting with naturally occurring (S)-citramalic acid (II). The authors have also used this procedure to synthesized the less active (S)-bicalutamide from the unnatural (R)-citramalic acid.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:359958 CAPLUS
DOCUMENT NUMBER: 134:366692
TITLE: Resolution of intermediates in the synthesis of enantiomeric bicalutamide and analogs
INVENTOR(S): Ekwuribe, Nnochiri N.; James, Kenneth D.
PATENT ASSIGNEE(S): Nobex Corporation, USA
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034563	A1	20010517	WO 2000-US41609	20001025
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000015124	A	20020702	BR 2000-15124	20001025
EP 1224167	A1	20020724	EP 2000-989719	20001025

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

JP 2003513955	T2	20030415	JP 2001-536512		20001025
US 6593492	B1	20030715	US 2000-695884		20001025
NZ 518552	A	20031031	NZ 2000-518552		20001025
ZA 2002003228	A	20030723	ZA 2002-3228		20020423
NO 2002001999	A	20020620	NO 2002-1999		20020426
PRIORITY APPLN. INFO.:			US 1999-161884P	P	19991027
			WO 2000-US41609	W	20001025

OTHER SOURCE(S): MARPAT 134:366692

IT **339530-92-6P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(resolution of intermediates in the synthesis of enantiomeric bicalutamide and analogs)

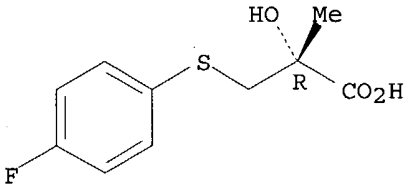
RN 339530-92-6 CAPLUS

CN Cinchonan-9-ol, (8α,9R)-, mono[(2R)-3-[(4-fluorophenyl)thio]-2-hydroxy-2-methylpropanoate] (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 335595-52-3
CMF C10 H11 F O3 S

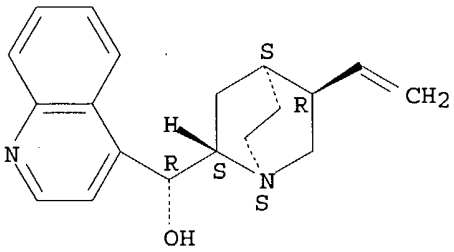
Absolute stereochemistry.



CM 2

CRN 485-71-2
CMF C19 H22 N2 O

Absolute stereochemistry.

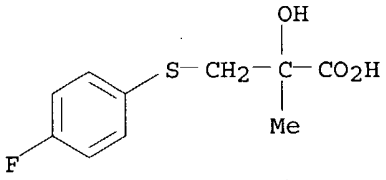


IT **339530-91-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(resolution of intermediates in the synthesis of enantiomeric bicalutamide and analogs)

RN 339530-91-5 CAPLUS

CN Propanoic acid, 3-[(4-fluorophenyl)thio]-2-hydroxy-2-methyl- (9CI) (CA

INDEX NAME)

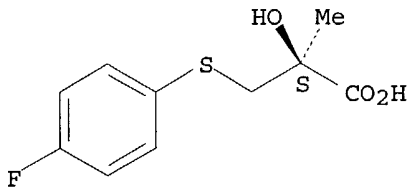


IT **339530-94-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(resolution of intermediates in the synthesis of enantiomeric bicalutamide and analogs)
RN 339530-94-8 CAPLUS
CN Cinchonan-9-ol, (8α,9R)-, mono[(2S)-3-[(4-fluorophenyl)thio]-2-hydroxy-2-methylpropanoate] (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 339530-93-7
CMF C10 H11 F O3 S

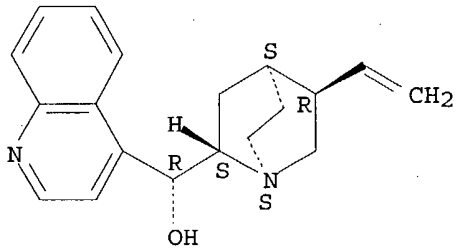
Absolute stereochemistry.



CM 2

CRN 485-71-2
CMF C19 H22 N2 O

Absolute stereochemistry.



AB Title enantiomeric acylanilides were prepared by resolution of R4ZZ1Z2CR1(OH)CO2H [R1 = (halo)alkyl; R4 = (hydroxy)alkyl, alkenyl, (un)substituted Ph, etc.; Z = bond or alkylene; Z1 = O, SO0-2, (alkyl)imino; Z2 = alkylene] followed by amidation.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:300671 CAPLUS
DOCUMENT NUMBER: 134:326279
TITLE: Asymmetric synthesis and antiandrogenic use of enantiomers of Casodex (bicalutamide) and derivatives from enantiomers of citramalic acid or proline.
INVENTOR(S): Ekwuribe, Nnochiri
PATENT ASSIGNEE(S): Nobex Corporation, USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001028990	A2	20010426	WO 2000-US41233	20001018
WO 2001028990	A3	20010907		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1222165	A2	20020717	EP 2000-982690	20001018
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
BR 2000014889	A	20021231	BR 2000-14889	20001018
JP 2003512351	T2	20030402	JP 2001-531790	20001018
US 6583306	B1	20030624	US 2000-691621	20001018
NZ 518392	A	20040227	NZ 2000-518392	20001018
ZA 2002002947	A	20030715	ZA 2002-2947	20020415
NO 2002001831	A	20020619	NO 2002-1831	20020418
US 2004030130	A1	20040212	US 2003-444343	20030523

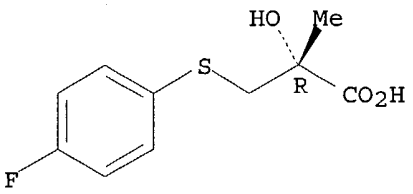
PRIORITY APPLN. INFO.: US 1999-160412P P 19991019
US 2000-691621 A3 20001018
WO 2000-US41233 W 20001018

OTHER SOURCE(S): CASREACT 134:326279; MARPAT 134:326279

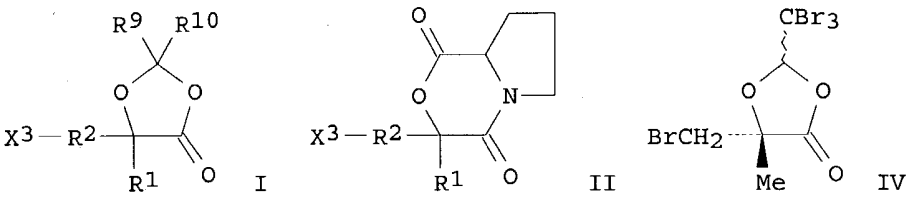
IT **335595-52-3P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(asym. synthesis (and use) of (R)- and (S)-Casodex (bicalutamide) from (S)- and (R)-citramalic acid)

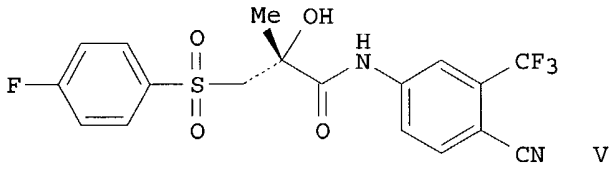
RN 335595-52-3 CAPLUS
CN Propanoic acid, 3-[(4-fluorophenyl)thio]-2-hydroxy-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI

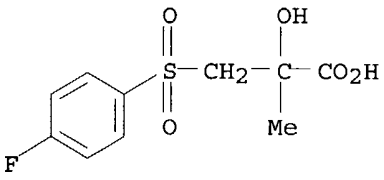




AB A method of synthesizing pure enantiomers of acylanilides such as Casodex (bicalutamide) is disclosed. The method involves contacting certain ring compds. including I, II, or similar gem-disubstituted epoxides with nucleophiles R7-R6-X1H under conditions sufficient to provide a compound R7-R6-X2-R2-C(OH)(R1)-CO2H [wherein; R1 is alkyl or haloalkyl up to C4; R2 is alkyl up to C6; R6 is a bond or alkyl up to C6; R7 is alk(en)yl, hydroxyalkyl, etc. or R7 is Ph (substituted with up to 3 substituents chosen from H, halo, nitro, carboxy, carbamoyl, etc.); X1 is O, SO0-2, or (alkyl)imino; X2 is O, S(O)0-2 or (oxidized)(alkyl)imino; X3 is a leaving group]. The starting ring compds. are those that, when opened, provide a substituent -R2-C(OH)(R1)-R3 [wherein; R3 is CH2OR4, where R4 is H, PhCH2, C(O)CH3, C(O)OR5, where R5 is H or alkyl]. In an exemplary embodiment, readily available (S)-citramalic acid is reacted with bromal to yield I (R9 = H, R10 is CBr3, R1 is β-Me, R2 is α-CH2 and X3 is CO2H; III). Compound III is condensed with 2-mercaptopyridine-N-oxide using DCC in CBrCl3 (solvent) at reflux which resulted in α-bromination/decarboxylation to IV. Intermediate IV was sequentially treated with base and 4-fluorobenzenethiol, coupled with 4-amino-2-trifluoromethylbenzonitrile and oxidized with mCPBA to give (R)-Casodex (V). The order of steps in the conversion of I or II to compds. exemplified by V may vary (e.g. substitution and oxidation of a sidechain of I may precede ring opening). The conversion of (R)-citramalic acid to (S)-Casodex is also claimed. Addnl., the invention mentions a modification of a route previously described for the

transformation of (R)- and (S)-proline to (R)- and (S)-Casodex that improves yield proceeding through a proline-derived intermediate II. Biol. data comparing (R)-, (S)- and (±)-Casodex, synthesized by this method, in lowering testosterone response showed (R)-Casodex to be substantially more potent than the (S)-isomer.

L4 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:640883 CAPLUS
DOCUMENT NUMBER: 119:240883
TITLE: Metabolism of Casodex in laboratory animals
AUTHOR(S): Boyle, G. W.; McKillop, D.; Phillips, P. J.; Harding, J. R.; Pickford, R.; McCormick, A. D.
CORPORATE SOURCE: Saf. Med. Dep., ICI Pharm., Alderley Park/Macclesfield/Cheshire, SK10 4TG, UK
SOURCE: Xenobiotica (1993), 23(7), 781-98
CODEN: XENOBH; ISSN: 0049-8254
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **151262-57-6**
RL: FORM (Formation, nonpreparative)
(formation of, as Casodex metabolite, species differences in)
RN 151262-57-6 CAPLUS
CN Propanoic acid, 3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl- (9CI) (CA INDEX NAME)



AB Casodex, a non-steroidal antiandrogen, was eliminated primarily in feces by rat, mouse, rabbit and dog. Rat, mouse and rabbit eliminated 20-30% of a single oral dose (8-25 mg/kg) in urine; only 3-4% was excreted in urine by dog (2.5 mg/kg). Oral absorption was about 80% in rat, mouse, rabbit and dog. Most of the dose was recovered in 48 h from rat, mouse and rabbit. In rat, <1% of the dose was exhaled as 14CO2 and <1% remained in the carcass after 7 days. Recovery from dog was incomplete in 4 days but consistent with the long plasma elimination half-life of 7-7.5 days. Casodex was eliminated from rat plasma with a half-life of 17-21 h. Examination of urine indicated extensive metabolism of Casodex and showed a marked species difference. In rat, mouse and dog. Casodex was cleaved at the amide to yield a carboxylic acid and an aromatic amine which subsequently underwent ring hydroxylation with sulfate conjugation. In rabbit, the major urinary metabolite was Casodex glucuronide, conjugated on the tertiary hydroxyl. The major component in feces of all species was unchanged Casodex; some hydroxy-Casodex was also observed in rat feces. Anal. of rat and dog bile indicated that Casodex and hydroxy-Casodex were eliminated in bile primarily as glucuronide conjugates.

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	33.76	189.39

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-4.90	-4.90

STN INTERNATIONAL LOGOFF AT 15:01:31 ON 22 SEP 2004